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Acute Coronary Syndromes

ANNEXATM-R: A PHASE 3 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL, DEMONSTRATING REVERSAL OF RIVAROXABAN-INDUCED ANTICOAGULATION IN OLDER SUBJECTS BY ANDEXANET ALFA (PRT064445), A UNIVERSAL ANTIDOTE FOR FACTOR XA (FXA) INHIBITORS

Oral Contributions
Room 20A
Monday, March 16, 2015, 11:30 a.m.-11:42 a.m.

Session Title: Highlighted Original Research: Acute Coronary Syndromes and the Year in Review
Abstract Category: 2. Acute Coronary Syndromes: Clinical
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Background: Direct fXa inhibitors have become an important therapeutic option due to their advantages in efficacy and safety. However, bleeding remains the major adverse effect and there is no specific antidote for reversal in cases of serious bleeding episodes or prior to urgent/emergency surgery. Andexanet alfa (AnXa, PRT064445) is a modified, recombinant human fXa molecule that is catalytically inactive but retains high-affinity binding to direct and indirect fXa inhibitors. AnXa acts as a fXa decoy and reverses fXa inhibitor-mediated anticoagulation. We have previously reported randomized Phase 2 data in healthy subjects anticoagulated with apixaban, rivaroxaban or enoxaparin, where AnXa rapidly and significantly reversed anti-fXa activity and the inhibition of thrombin generation. Here we report data from the first Phase 3 registration study of AnXa administered to older subjects anticoagulated with rivaroxaban.

Methods: ANNEXA™-R is a Phase 3, double-blind, placebo-controlled study of AnXa in older subjects treated with rivaroxaban. Part 1 of the study investigated a bolus regimen and Part 2 will investigate a bolus followed by a 2 hour continuous infusion. In Part 1, 39 subjects age 50 to 75 were randomized to receive either AnXa or placebo in a 2:1 ratio. All subjects received rivaroxaban 20 mg PO QD for 4 days. AnXa at a dose of 800 mg IV bolus or placebo was administered on Day 4, 4 hours after the last rivaroxaban dose (approximate rivaroxaban Cmax). Safety data were collected through Day 43. The primary efficacy endpoint is the reversal of rivaroxaban-induced anti-fXa activity (mean change from baseline at 2 or 5 min after the end of the bolus). Additional efficacy endpoints included reduction in plasma free fraction of rivaroxaban and restoration of thrombin generation.

Results and Conclusion: Part 1 of the pivotal Phase 3 study has been completed. Final efficacy and safety results for Part 1 will be presented and discussed.